

REMARKS

Prior to this Response, claims 4-10 were pending in this application. Claims 1-3 and 11-21 were previously withdrawn under a restriction requirement. Claim 4 has been amended. These amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the amendment to claim 4 is found in Example 3 at page 11, paragraph 2; in claims 1-21 as originally filed; and elsewhere throughout the specification and claims. Accordingly, entry of the amendments is respectfully requested.

1. Objection to the Specification

The Office Action objects to the specification for the following reasons:

The disclosure is objected to because of the following informalities: Specification contains some empty spaces as intended for disclosure of IDA (International Depository Authority in accordance to the Budapest Treaty) accession numbers of the applicants' mutants characterized by high level of phytase activity. Appropriate correction is required.

As suggested by the Examiner, Applicants will amend the Specification to provide the MTCC accession numbers of the Applicants' mutants when such numbers become available, such amendment to be made in a Supplemental Response. It is respectfully requested that before issuing a further Office Action relating to this point, the Examiner is encouraged to call Applicants' counsel if a Supplemental Response has not been filed by the time that this

application receives further examination.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the objection to the specification upon receipt of a Supplemental Response.

2. Rejections under 35 U.S.C. §112, first paragraph

The Office Action rejects claims 4-10 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, and states the following:

At least some of the claims require one of ordinary skill in the art to have access to "yeast mutants" derived from a parent strain MTCC 5155 (CFR 505) belonging to the species of *Candida versatilis*. Because these "mutants" are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the "mutants" are not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by deposit of these microorganisms. The specification does not disclose a repeatable process to obtain the microorganisms and it is not clear from the specification or record that the microorganisms are readily available to the public.

For example: the disclosed mutants EMY 505 and UVY 505 that are characterized by the claimed phytase activity ranging between 140 U/g and 197 U/g are obtained by mutagenization of the claimed strain MTCC 5155 (same as CFR 505) and the method of making the mutants EMY 505 and UV 505 by mutagenization is clearly unpredictable (example 2, specification pages 8-10). The claimed parent strain MTCC 5155 (same as CFR 505) fails to reduce phytic acid level in dough as disclosed (specification page 11,

last par.).

The instant rejection may be overcome by establishing that each microorganism identified is readily available to the public and will continue to be so for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, or by an acceptable deposit as set forth herein. See 37 CFR 1.801-1.809.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or a statement by an attorney of record over his/her signature and registration number, stating that the deposit has been made under the Budapest Treaty and that all restrictions imposed by the depositor on availability to the public of the deposited material will be irrevocably removed upon issuance of the patent would satisfy the deposit requirement. See 37 CFR 1.808.

Applicants' counsel, on behalf of Applicants, hereby states the following: Under 37 CFR 1.808, Applicants affirm that the deposit of biological materials of mutants of strain CFR 505/MTCC 5155 has or will be been made under the Budapest Treaty to the MTCC in India, and that all restrictions imposed by the depositor on availability to the public of the deposited material will be irrevocably removed upon issuance of a patent in this matter. Applicants will provide the MTCC accession numbers and a Declaration to this effect upon receipt of the MTCC accession numbers.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

3. Rejections under 35 U.S.C. §112 for Indefiniteness

The Office Action rejects claims 4-10 under 35 U.S.C. § 112, second paragraph, for the following reasons:

Claim 4 is rendered indefinite, uncertain, confusing and improper by the phrase "strain comprising yeast mutants" as presently recited in the step (c) in the method of making dough. The microbial strain is a specific entity by itself and the mutants derived from one parent strain will be some other strains distinct from the patent strain. The terminology used in the claim is inconsistent with the art accepted meaning.

In the light of the as-filed specification it appears that the presently claimed phrase "obtaining a mutated, permeabilized strain of a yeast *Candida versatilis* MTCC 5155, said strain comprising yeast mutants having phytase activity ranging between 140 U/g and 197 U/g" is intended to mean "obtaining a mixture of permeabilized yeast cells having phytase activity ranging between 140 U/g and 197 U/g wherein the yeast cells belong to *Candida versatilis* strain EMY 505 or to *Candida versatilis* strain UYV 505". See specification page 10, par. 2. The parent strain MTCC 5155 as disclosed does have phytase activity ranging between 140 U/g and 197 U/g as claimed. The parent strain is distinct from its mutants by morphology as disclosed by applicants (page 10. lines 1-2) and by phytase activity (page 11, par. 2 and page 10. par. 2).

Applicants respectfully submit that the foregoing claim amendments obviate these rejections.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

4. Rejection of Claims 4-10 under 35 U.S.C. §112 for New Matter

The Office Action rejects claims 4-10 under 35 U.S.C. §112, second paragraph, for the following reasons:

Insertion of the limitation drawn to the use of an yeast strain "MTCC 5155" "having phytase activity ranging between 140 U/g and 197 U/g" that has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus that would show possession of the concept of the use of the specific yeast strain "MTCC 5155" with "phytase activity ranging between 140 U/g and 197 U/g" in order to obtain dough with 10-40% reduction in the level of phytic acid.

Applicants respectfully traverse this rejection. Claim 4 as presently presented is drawn to mutant strains derived from parent strain *Candida versatilis* MTCC 5155, that is strains UY 505 and EY 505 having phytase activity in the range of 140 U/g and 197 U/g respectively; and not to the parent strain MTCC 5155. The specification also supports the claimed activity ranges (Example 3, page 11, paragraph 2).

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

5. Rejection of Claims 4-10 under 35 U.S.C. §103(a)

The Office Action rejects claims 4-10 under 35 U.S.C. §103(a) as being unpatentable over US 4,794,014 (Siren), Quan et al. ("Production of phytase in a low phosphate medium by a novel yeast *Candida krusei*". Journal of Bioscience and Bioengineering. 2001. Vol. 92, No. 2, pages 154-160) and Bindu et al. ("A comparative study on permeabilization treatments for in situ determination of phytase of *Rhodotorula gracilis*". Letters in Applied Microbiology.

1998. 27:336-340). As the basis for this rejection, the Office Action states, in relevant part:

The cited patent US 4,794,014 (Siren) discloses a method for reducing phytic acid level in food preparations made from phytate-containing materials (IP6 materials) by using yeast cells as a source of phytase (entire document including col. 3, lines 50-65 and col. 5, lines 22-24). The starting IP6 materials include wheat, wheat bran and wheat flour. In particular example the method for reducing phytic acid level comprises step of making dough by mixing wheat flour, water, salt and the yeast strain(s) and storing the dough, thereby, obtaining reduction in the level of phytic acid (examples 4 and 8). The cited patent teaches that phytate hydrolysis occurs at temperature ranges 20-70°C, thus, including the presently claimed temperatures. The yeast culture that is used as a source of phytase is generic and/or belongs to baker's yeast or *Saccharomyces*. Thus, the cited patent is lacking particular disclosure about the use of yeast cells belonging to *Candida*.

However, the reference by Quan et al. demonstrates that yeast cells belonging to *Candida* produce high level of phytase (abstracts) and they are capable of biodegrading phytate in food materials including wheat. In particular example wheat phytate is biodegraded or phytate amounts are considerably reduced within 12 hours (fig. 7 and page 159, col. 1, par. 1).

The cited documents US 4,794,014 (Siren) and Quan et al. demonstrate that yeast cells are source of phytase but they are silent about preliminary treatments of yeast cells that are used as source of phytase in the methods for reducing phytic level in food preparation including wheat and/or wheat-containing dough.

However, the reference by Bindu et al. teaches that yeast cells have tough cell walls, that permeabilization treatments provide for a larger amount of released enzymes and that repeated cycles of freeze-thawing are most efficient for enhancing phytase activity in yeast cell preparations (entire document including abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify method for reducing phytic

acid level taught by US 4,794,014 (Siren) by using yeast cells belonging to Candida with a reasonable expectation of success in reducing phytic acid level in wheat containing food including dough or "Chapathi dough" because it is well known that yeast cells are used for enzymatic reduction of phytic acid levels in various food and that yeast cells belonging to Candida are source of phytase having high enzymatic activity. One of skill in 'the art would have been motivated to enhance enzymatic activity of yeast cell preparations by permeabilizing yeast cells through repeated freeze-thaw cycles for the expected benefits in increasing levels of phytate biodegradation.

RESPONSE

Applicants respectfully traverse this rejection as failing to teach or suggest all the limitations of the present claims.

To establish a *prima facie* case, the PTO must satisfy three requirements. First, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970). Second, as the U.S. Supreme Court recently held in KSR International Co. v. Teleflex Inc. et al., Slip Opinion No. 04-1350, 550 U. S. ____ (April 30, 2007), "a court must... determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (KSR,

supra, slip opinion at 13-15; emphasis added.) Lastly, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Fed. Cir. 1991).

The presently claimed subject matter relates to a method of using a mutated, permeabilized strain *Candida versatilis* MTCC 5155 in optimizing the making of traditional *Chapathi* dough, by improving the process of reducing phytic acid and increasing the bioaccessibility of nutrients, thus improving the nutritional value of the *Chapathi*, as was discussed in detail in the Response filed October 1, 2007.

U.S. patent 4794014 (Siren), discloses a method to reduce phytic acid content in food. However, the precise parameters and conditions used in the instant application are completely distinct, specifically the ratio of water to wheat flour used in the two inventions are very different. Additionally Siren uses salt concentration that is beyond the concentration as disclosed in the present invention. Moreover, Siren only presents a very general view of the method of reducing phytic acid content by utilizing a generic yeast strain, Bakers Yeast or *Saccharomyces*.

However, Siren is silent over specifically the ability of the strain *Candida versatilis* MTCC 5155 and its mutants to reduce phytate levels, as disclosed and claimed in the present invention.

Further, the Examiner also points out that Siren discloses a temperature range of 20-70°C for phytate hydrolysis. It is generally very well known that enzymes function at their highest catalytic efficiency at a particular temperature, designated as the temperature optima. The temperature range as disclosed in Siren is too broad for the enzyme to function efficiently, specifically for an enzyme from a mesophilic source. Although Arrhenius kinetics suggests use of the highest 'feasible' temperature for enzyme function, in practice the use of high temperature ranges is normally restricted because of the highly unstable and labile disposition of enzymes. An enzyme from a mesophilic source, as in the present case, would exhibit stability and activity in the mesophilic temperature ranges and likely be denatured at high temperature like 70°C, since it is not under any evolutionary pressure to be active at such high temperatures. Likewise, an enzyme from a thermophilic source would exhibit reduced reaction rates at mesophilic temperatures and be highly active at high temperatures. This is due to the fact that thermophilic proteins have evolved to perform their catalytic function at such high temperatures. However, the temperature range disclosed in the present invention is specific and it is within this range that the enzyme exhibits highest activity.

In light of these deficiencies, the Examiner further cites Quan, et al. Quan, et. al. mentions that the specific yeast strain

C. krusei possesses high phytase activity. However, Quan, et. al. is silent over the use of the species *C. versatilis* or specifically mutants of the strain *Candida versatilis* MTCC 5155 as a source of phytase.

Therefore, Quan, et. al. and Siren, taken together, fail to make it obvious to a skilled person that the strain *Candida versatilis* MTCC 5155 and its mutants exhibit high enzyme activity and can also be used as a source of highly active phytase. Additionally, both Quan, et. al. and Siren do not teach or suggest the need to develop mutants of the parent strain to achieve enhanced enzyme activity. Quan, et. al. and Siren, alone or taken together, do not also teach or suggest preliminary cell permeabilization to improve substrate accessibility, in order to overcome mass transfer limitations.

In light of these deficiencies, the Examiner further cites Bindu et. al. Bindu et. al. disclose a study on cell wall permeabilization of the yeast *Rhodotorula gracilis*. However, it is well known that each microorganism is distinct from another in genetic makeup, and therefore it is not predictable that distant and distinct yeast species might have similar characteristics. It is generally well known that each cell type requires a unique combination of growth conditions and growth medium components for the expression of a particular phenotype, and indeed may even differ in cell wall composition.

The yeast strains of the genus *Rhodotorula* and the genus *Candida* are distinct from one another. The fact that the permeabilization method disclosed in the cited document of Bindu et. al. works well for *Rhodotorula gracilis* does not in any way render obvious the use of the same method for permeabilization of *Candida versatilis* MTCC 5155 and its mutant strains.

Individually or taken together, Quan, et. al., Siren, and Bindu et. al. fail to teach or suggest a reason to develop highly active mutants of a *Candida* genus or specifically *Candida versatilis* MTCC 5155 species and its mutants. At best, the cited references teach only that some yeast genres can be used to make chapathi dough. However, in the absence of the hindsight use of Applicants' disclosure, the references cited fail to teach any of the following features of the present invention:

1. the selection of a base yeast species which is not taught by the prior art,
2. the creation and selection of a mutant yeast species, neither of which is taught by the prior art,
3. the selection of a limited temperature range which is not taught by the prior art,
4. the selection of a ratio of water to wheat flour which is not taught by the prior art,
5. the selection of a salt concentration which is not taught by the prior art, and

6. the selection of a permeabilization method which is not taught by the prior art.

Thus, in order to reach the claimed invention, the teachings of the prior art must not only be simply *combined*, but then the combined teachings must also be *significantly modified*. Contrary to the Office Action, the cited references at best teach the generic state of the art prior to the present invention, and fail to teach or suggest any reason to make the many modifications to the prior art that are required to reach the present invention.

As discussed previously, the claimed subject matter relates to an improvement on the prior art, the use of mutant *Candida versatilis* **strain** MTCC 5155 avoids several drawbacks found in prior art methods. Again, the cited references do not teach or suggest either: (1) generally, the use yeast strains of the **species** *Candida versatilis*, (2) specifically the particular mutant **strains** derived from MTCC 5155, nor (3) any suggestion to make a *Candida versatilis* strain which is genetically modified to avoid the described drawbacks in the prior art.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is believed to be clear and definite, fully enabled, and

patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of remaining claims 4-10 and allow all pending claims presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

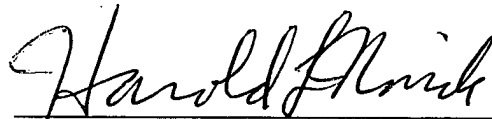
The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,

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